1 Introduction

Recent trends in the biopharmaceutical industry derived from technological advances (e.g., increased drug potency and smaller *niche* markets targeting patient-specific drugs) have resulted in the need for flexible manufacturing facilities. Further achievements in engineering cell lines capable of high production titres has led to a decrease in the volumetric manufacturing capacity needed to align with market requirements. Concurrently, the previous decade has seen the development of single-use technologies (SUT) applicable to biopharmaceutical manufacturing from the simplest and widely used bag systems and filters to more complex systems such as bioreactors, chromatography and fill-finish operations. As a result, industrial adoption of SUT has increased gradually, and end-users are considering application of the technology to operations discounted previously due to technical or scale limitations. Increased adoption of SUT has also brought about the realisation that new challenges are encountered to select, specify, implement and maintain the technology throughout the lifecycle of the active pharmaceutical ingredient (API). This handbook has been written to provide practical guidance on: (i) considerations for the end-user to review while choosing technologies to apply to processes; and (ii) implementation of SUT.

The route by which a process for the manufacture of biological products is designed, implemented and qualified can be long and complex. It requires the input of multi-disciplinary teams and there are many risks of failure. For example, the process can fail if it cannot be controlled to provide reliable batch-to-batch consistency of the product with sufficient quality. Exposure to risks by a particular organisations is dependent upon its experience with the product, process, manufacturing technologies and scale of operation. Many single-use systems are considered to be 'mature' because they have been present on the market for >10 years, been through design changes to improve performance, and have been utilised across a wide range of scales and manufacturing scenarios, from clinical through to commercial. However, other SUT are 'immature' and require more time to implement due to limited knowledge, availability and adaptability of the technology. There are no standardised approaches for SUT implementation. Instead, the implementation strategy should be 'tailored' based upon the type of technology and level of expertise of the end-user.

Compared with traditional stainless-steel systems, additional risks must be considered when using SUT. A comprehensive list of these risks is shown in Table 1.1. They have been grouped based upon impact to the end-user, supply chain, material and process.

These risks illustrate the range of capabilities that end-users must possess within their organisation, or that they will need to leverage from the supplier or third-part service providers to implement SUT. Hence, some end-users continue to employ traditional stainless-steel systems that they have expertise with, or adopt a

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